Department of Sociology

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A Lifecourse Approach to Genetic Endowment and Cognitive Decline

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The Puzzle

- Cognitive status decline with age, but some people experience faster decline than others (Stern,2009)
- Educational attainment as cognitive reserve is related to better level of cognitive status
    - Improve problem solving, stress coping abilities
    - Improve effectiveness in using brain network
- Mixed evidence on education and rate of cognitive decline
- Education and cognitive ability has shared genetic bases (Okbay et al., 2016; Lee et al., in press)
- Current research seldom account for genetic markers

Research Questions

- How does the association between genetic endowment of education and rate of cognitive decline change with age among older adults (50+) in the US?
- After accounting for genetic endowments, what are the effects of sociodemographic and behavioral factors?

Three competing hypotheses

- Active reserve model:
  - Higher education, slower rate of decline (divergence)
- Passive reserve model:
  - Higher education has no effect on rate of cognitive decline (stable)
- Compensation model:
  - Higher education, faster rate of decline (Convergence)

Sample

- Health and Retirement Survey 1998-2012
  - a biennial, longitudinal survey of a nationally-representative sample of individuals and their spouses aged 50 and above.
  - Genetic information is collected in 2006 and 2008
- 5,005 European and non-Hispanic respondents with at least 4 cognitive interviews

DV – Cognitive Measure

- Episodic Memory (EM)
  - Encodes and retrieves personal experienced events occurred at specific time and place
  - Delayed word recall
- Working Memory (EM)
  - Remember and use memory while in the middle of an activity
  - Serial 7s subtraction test
- Mental status (MS)
  - Knowledge-related cognitive ability
  - naming the date, month, year and day of the week, backwards counting from 20, object naming, and naming the current president and vice president of the U.S.
- Vocabulary (Vocab)
  - Define 5 words
- Global cognition (GC)
  - Average corrected percentage score: (score/maximum score)*100

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PGS for individual i are calculated as the sum of the allele counts a_{ij} (0, 1, or 2) for each SNP $j = 1, \dots M$, weighted by association strength p_j:
$Polygenic\ score = \sum_{j=1}^{M} p_j a_{ij}$

- Polygenic score for education (Okbay et al., 2016), standadised
  - Inverse probability weight (Domingue et al., 2017)
- Years of schooling
- Gender, social interaction, health behavior, chronic diseases
- Analytical Strategy: Linear mixed models

$$Cognition_{ij} = \beta_0 + \beta_1 * Age_j + \beta_2 * PGSedu_i + \beta_3 * PGSedu_i * Age_j + \beta_4 * X_{ij} + \beta_5 * X_{ij} * Age_j + \mu_{ij} + \mu_{ij} * Age_j + \varepsilon_\iota$$

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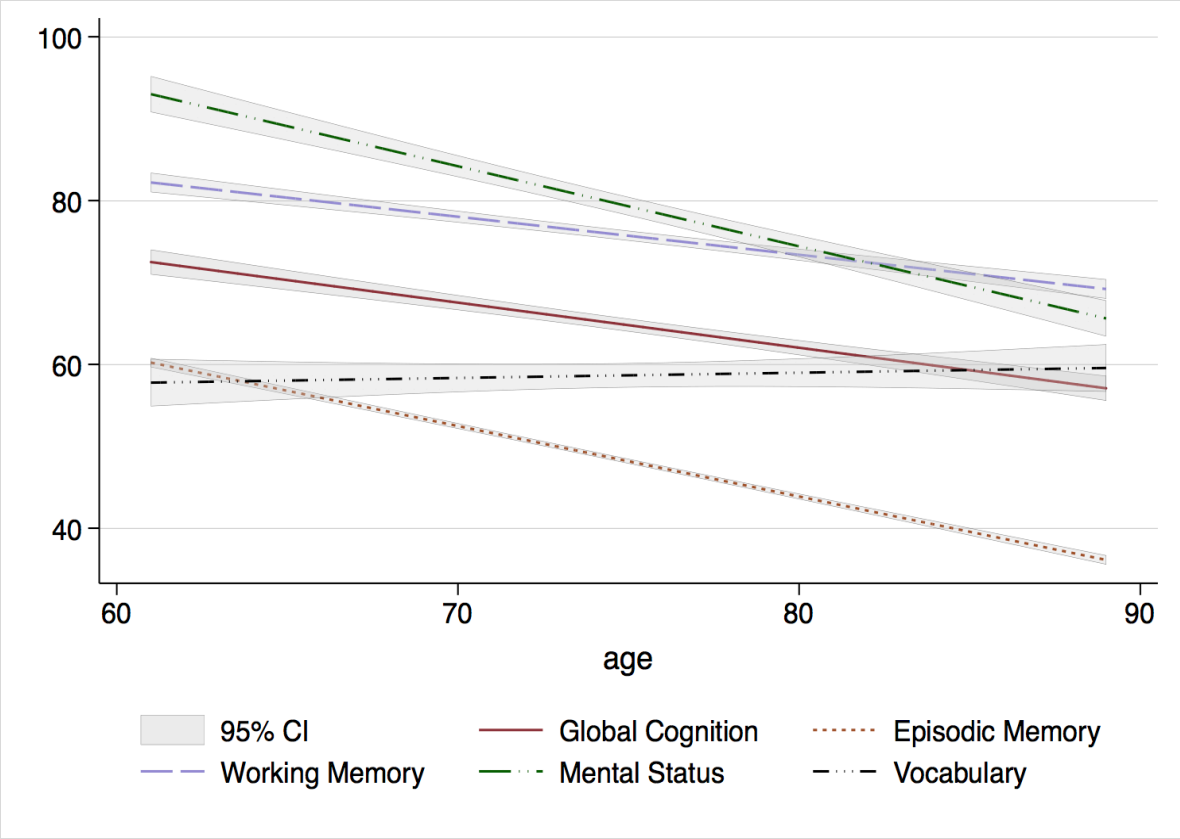
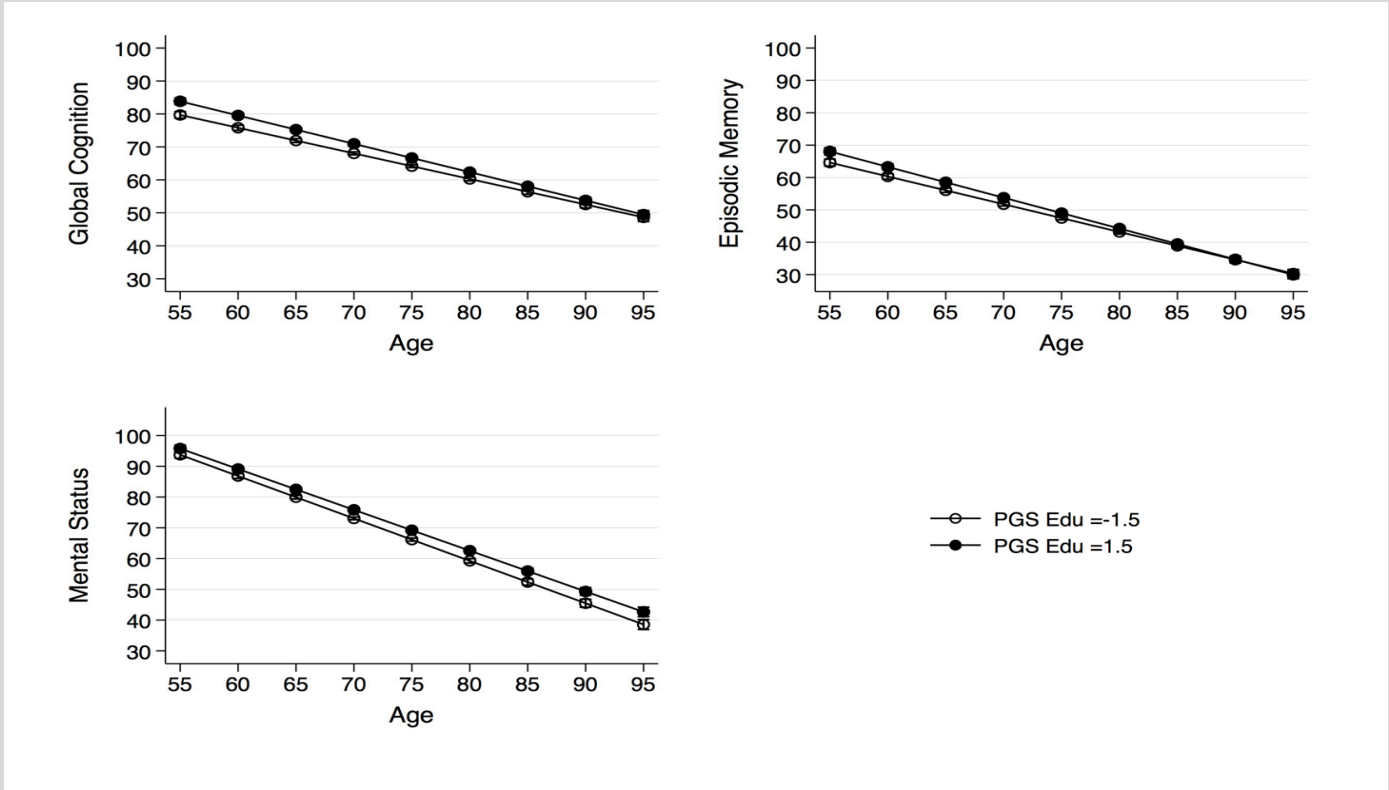
Results



Results – Linear Mixed Models

- Higher education polygenic score is associated with better cognitive performance (β Range from 0.08 – 2.44)
- PGS education on rate of cognitive decline varies across domains
  - Strength of association declines for EM, GC (Compensation);
  - Magnifies for MS (Active Reserve);
  - Remains constant for WM, and Vocab (Passive)

Results


Global Cognition
100
90
80
70
60
50
40
30
55 60 65 70 75 80 85 90 95
Age
Episodic Memory
100
90
80
70
60
50
40
30
55 60 65 70 75 80 85 90 95
Age
Mental Status
100
90
80
70
60
50
40
30
55 60 65 70 75 80 85 90 95
Age
PGS Edu =-1.5
PGS Edu =1.5

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Results

- Women performs better in GC, EM, Vocab, worse in WM, no difference in MS. Women also decline faster in GC, EM, WM.
- Years of schooling positively related to cognitive ability, but is associated with faster decline in EM, MS, and slower decline in WM.
- Social interaction: slower decline in GC, EM and MS.
- Smoking: faster decline in MS.
- Multi-morbidity in chronic diseases: faster decline in all measures.

Discussion

- Is the result due to insufficient control? (Keller, 2014)
- Limitations: floor and ceiling effect, mechanisms from a biological angle, other race and ethnicity.